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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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KLARQUIST SPARKMAN, LLP
121 S.W. SALMON STREET, SUITE #1600
ONE WORLD TRADE CENTER
PORTLAND, OR 97204-2988

EXAMINER

HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 12/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/830,748

Applicant(s)

KASHMIRI ET AL.

Examiner

Larry R. Helms

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4,6,10-13,15,17,19,21-24,26,28,30,34,35,38,40,41 and 48-69 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1,2,4,6,10-13,15,17,19,21-24,26,28,30,34,38,40,41 and 48-69 is/are rejected.
- 7) ☒ Claim(s) 35 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Claims 1-2, 4, 6, 10-13, 15, 17, 19, 21-24, 26, 28, 30, 34-35, 38, 40-41, 48-69 are pending.

Claims 1-2, 4, 6, 10-11, 15, 17, 19, 23, 26, 28, 30, 34, 53, 57, 69 have been amended.

2. Claims 1-2, 4, 6, 10-13, 15, 17, 19, 21-24, 26, 28, 30, 34-35, 38, 40-41, 48-69 are under examination.

3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

Rejections Withdrawn

4. The rejection of claims 10, 34-35, 53, 57, and 69 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

5. The rejection of claims 1-2, 4, 6, 10-13, 15, 17, 19, 21-24, 26, 28, 30, 38, 40-41, 48-49, 51-55, 57-64, 66-69 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendments to the claims.

6. The rejection of claims 1-2, 4, 6, 10-13, 15, 17, 19, 21-24, 26, 28, 30, 34-35, 38, 40-41, 48-69 under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence

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that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description is withdrawn in view that the amino acid sequences of the CC49 antibody is given in the specification and the claims only require the CDRs from the CC49 antibody.

Response to Arguments

7. The rejection of claim 58 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

The response filed 9/19/03 has been carefully considered but is deemed not to be persuasive. The response states that claim 58 depends from claim 24 and claim 24 requires the positions at least one of 60, 61, 62, or 64 to be human residues from 21/28'CL and claim 58 recites human positions at positions 12, 13, 14, or 16 as in SEQ ID NO:11 and these corresponding amino acids replace the murine amino acids at positions 60, 61, 62, or 64. (see page 11-12 of response). In response to this argument, it is still not clear if the murine residues that are replaced at positions 60, 61, 62, or 64 are those at positions 12, 13, 14, or 16 in SEQ ID NO:11 or if residues 12, 13, 14, or 16 are additionally human residues in addition to 60, 61, 62, or 64.

8. The rejection of claims 1-2, 4, 6, 10-13, 15, 17, 19, 21-24, 26, 28, 30, 34, 38, 40-41, 48-69 under 35 U.S.C. 103(a) as being unpatentable over Mezes et al (U.S. Patent 6,495,137, filed 10/97) and further in view of Padlan et al (FASEB J. 9:133-139, 1995,

IDS #11) and as evidenced by Tamura et al (The Journal of Immunology 164:1432-41, 2000, IDS #13) is maintained.

The response filed 9/19/03 has been carefully considered but is deemed not to be persuasive. The response states that unexpectedly only the replacement of specific CC49 CDRs with LEN resulted in reduction of immunogenicity and replacement of only CDR1 and 2 of the light chain with LEN resulted in a slight reduction in immunogenicity compared to replacement of heavy chain CDRs and it is only applicants work that identifies the CDRs to alter (see page 14 of response). The response states that neither the 137 patent or Padlan suggest specific amino acids to be substituted or substitution of murine CDR residues and there is no specific teaching in Padlan to substitute murine CDRs with residues from LEN or 21/28'CL and Padlan acknowledges that SDRs are probably unique to each antibody and may only be possible to identify with the 3D structure of the complex with antigen (see page 15 of response). The response states that only the combination of all four amino acid substitutions resulted in binding affinity that was almost twice that of the parent and Tamura does not indicate that the prior art makes obvious which amino acid should be replaced. (see page 16-17 of response). In response to these arguments, the argument that replacement of CDR1 and 2 with LEN was unexpected is not commensurate in scope with claims 11, 23, 34 and those dependent on these claims because these claims do not necessarily result in replacement of any entire CDR with LEN sequences. As to the replacement of CDR1 and 2 of the light chain with LEN, Padlan does teach that the three dimensional structure may be needed, however, his study is with numerous antibody amino acid

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sequences which it is known that antibodies have a conserved three dimensional structure and as such from Padlans work he concludes that in CDRL1 for 17 residues only 27d may be important (see Table 4) and in CC49 and LEN, as evidenced from Tamura Table 1, this residues is the same in both and as such one would replace the CDRL1 with LEN because it reduces the immunogenicity. As far as CDRL2 is concerned, Padlan teach that for 7 residues only residue 50 and 55 may be important and again these two residues are the same in LEN CDRL2. It would have been obvious to substitute CDRL2 of LEN for CDRL2 of CC49 for reduction of immunogenicity. In addition, it would have been obvious to use LEN and the 21/28'CL residues and LEN CDRs because Mezes et al teach humanization with these human light and heavy chains due to their high homology with the CC49 amino acid sequence (see column 39-40). Mezes et al in combination with Padlan et al would result in picking LEN and 21/28'CL and analysis using Padlans method would result in replacing CDRL1 and CDRL2 with LEN as discussed above. One would also be motivated and had a reasonable expectation of success to substitute residues 60, 61, 62, or 64 of CC49 with those in 21/28'CL because Padlan again teach that in 17 residue CDRH2 (see Table 5) these residues are not highly variable and as such these residues can be of human origin of 21/28'CL which as taught by Mezes was the heavy chain variable region chosen for humanization. In addition residue 97 as taught by Padlan would also be human in the light chain and as evidenced by Tamura this residue is serine (see claim 34). Arguments directed to increased affinity by replacement of residues 97, 60-62, 64 is not commensurate in scope with the claims because the claims do not require

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increased binding. In addition, although it appears that increased affinity is achieved by replacement of these residues, the claims only require reduced immunogenicity and as such Padlan teach these residues need to be human for reduced immunogenicity.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

9. No claim is allowed. Claim 35 is objected to for depending on a rejected claim but would be allowable if rewritten in independent form from claim 34.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879



LARRY R. HELMS, PH.D
PRIMARY EXAMINER